We claim:

1. A method of reducing undesired light emission from a sample, comprising:

contacting a sample in need of reducing undesired light with at least one photon reducing agent,

wherein said sample comprises a membrane compartment in contact with a solid surface,

wherein said membrane compartment includes at least one photon producing agent and said at least one photon reducing agent is in an aqueous solution that contacts an outer surface of said membrane compartment, and

detecting an optical signal from said at least one photon producing agent.

2. The method of claim 1,

wherein said at least one photon reducing agent has an absorption spectra that overlaps with the absorption, emission or excitation spectrum of said at least one photon producing agent.

3. The method of claim 2,

wherein said at least one photon producing agent exhibits fluorescence resonance energy transfer with said at least one photon reducing agent.

4. The method of claim 3,

wherein said at least one photon reducing agent is present in said sample at a concentration between about 0.1 mM and about 0.5 mM.

5. The method of claim 2,

wherein said at least one photon reducing agent is substantially membrane impermeant.

6. The method of claim 1,

wherein said sample comprises at least two photon reducing agents.

7. The method of claim 6,

wherein at least one of said at least two photon reducing agents are dyes.

8. The method of claim 3,

wherein said membrane compartment comprises at least one living cell.

9. The method of claim 8,

wherein said at least one living cell is a mammalian cell.

10. The method of claim 1,

wherein said at least one photon reducing agent is selected from the group consisting of a collisional quencher, a particulate, an absorption quencher, a FRET quencher and a dark complex.

11. The method of claim 1,

wherein said at least one photon reducing agent is a dye.

12. The method of claim 8,

wherein said at least one living cell is part of a plurality of cells comprising at least two different photon producing agents.

13. The method of claim 9,

wherein said at least one photon producing agent corresponds to an enzyme activity inside said mammalian cell.

14. The method of claim 13,

wherein said at least one photon producing agent measures beta- lactamase activity.

15. The method of claim 14,

wherein said mammalian cell is one of at least 100 living cells.

16. The method of claim 9,

wherein said mammalian cell is a member of a clonal population of cultured cells.

17. The method of claim 1,

wherein said at least one photon reducing agent is more impermenant than said at least one photon producing agent across a membrane of said membrane compartment,

18. The method of claim 1,

wherein said detecting comprises detecting a fluorescence signal.

19. The method of claim 18,

wherein said at least one photon producing agent is produced from a precursor molecule that is a substrate for an esterase.

20. The method of claim 19,

wherein said at least one photon producing agent detects the presence of an ion inside said membrane compartment.

21. The method of claim 19,

wherein said at least one photon producing agent is a fluorescent protein.

22. The method of claim 21,

wherein said fluorescent protein is a modified green fluorescent protein.

23. The method of claim 19,

wherein said at least one photon producing agent detects voltage across a membrane of said membrane compartment.

24. A method of reducing light emission from a sample, comprising:

contacting a sample with at least one photon reducing agent,

wherein said sample comprises a membrane compartment,

further wherein said membrane compartment comprises at least one photon producing agent,

detecting a fluorescence signal from said sample,

wherein said at least one photon reducing agent is a dye and is present in said sample at a concentration that reduces undesired light emission from said sample by at least 30% compared to the light emission from said sample in the absence of said at least one photon reducing agent.

25. The method of claim 24,

wherein said light emission is not associated with said at least one photon producing agent located inside said membrane compartment.

26. The method of claim 25,

wherein said at least one photon reducing agent has a partition coefficient at a pH of about 7 equivalent or less than that of CCF2/AM.

27. The method of claim 24,

wherein said at least one photon reducing agent has an absorption spectra that overlaps with a portion of the emission or excitation spectrum of said at least one photon producing agent that is used to excite a FRET partner.

28. The method of claim 24,

wherein said at least one photon reducing agent has an extinction coefficient of at least 5,000 $M^{-1}cm^{-1}$.

29. The method of claim 28,

wherein said at least one photon reducing agent is not a pH indicator dye.

30. The method of claim 24,

wherein said at least one photon reducing agent has an absorption spectra that overlaps with the emission or excitation spectrum of said at least one photon producing agent.

31. The method of claim 30,

wherein said at least one photon reducing agent has an extinction coefficient of at least 5,000 $M^{-1}cm^{-1}$.

32. The method of claim 30,

wherein said sample comprises two different photon producing agents.

33. The method of claim 30,

wherein said sample has at least two photon reducing agents.

34. The method of claim 31,

wherein said at least one photon reducing agent comprises an azo dye.

35. The method of claim 24,

wherein said at least one photon producing agent is selected from the group consisting of an intracellular ion indicator, an enzyme substrate, a product of an enzyme reaction, a voltage sensor and a fluorescent protein.

36. The method of claim 24,

wherein said at least one photon producing agent is a fluorescent enzyme substrate or a fluorogenic enzyme substrate.

37. The method of claim 36,

wherein said at least one photon producing agent is an enzyme substrate for beta-lactamase.

38. The method of claim 33,

wherein said sample comprises an optical interferant.

39. The method of claim 24,

wherein said detecting comprises detecting epifluorescence from said sample.

40. The method of claim 39,

wherein said at least one photon reducing agent improves the optical signal to noise ratio by at least 300% compared to the optical signal to noise ratio of said sample in the absence of said at least one photon reducing agent.

41. The method of claim 39,

wherein said sample is present in a 384 well or greater sample format for said detecting.

42. The method of claim 41,

wherein said sample is about three microliters or less.

43. The method of claim 39,

wherein said method comprises contacting a test compound with a membrane of said membrane compartment.

44. The method of claim 43,

wherein said sample comprises a plurality of living cells and said contacting is prior to contacting said at least one photon reducing agent with said sample.

45. The method of claim 44,

wherein said sample comprises at least three photon producing agents.

46. The method of claim 44,

wherein said at least one photon producing agents is produced from a precursor molecule that is a substrate for an intracellular enzyme.

47. The method of claim 46,

wherein said intracellular enzyme is an esterase.

48. The method of claim 40,

wherein said sample comprises a test chemical that is an optical interferant.

49. A composition of matter, comprising:

a) a membrane compartment in contact with a solid surface, wherein said membrane compartment comprises at least one photon producing agent, and

b) an aqueous solution with at least one photon reducing agent, wherein said aqueous solution in contact with an outer surface of said membrane compartment.

50. The composition of matter of claim 49,

wherein said aqueous solution further comprises said at least one photon producing agent.

51. The composition of matter of claim 49,

wherein said at least one photon reducing agent is present in said aqueous solution at a concentration sufficient to reduce light emitted from said at least one photon producing agent present in said aqueous solution.

52. The composition of matter of claim 51,

wherein said at least one photon reducing agent has an absorption spectrum that overlaps with the absorption, emission or excitation spectrum of said at least one photon producing agent or said at least one photon producing agent in said aqueous solution exhibits fluorescence resonance energy transfer with said at least one photon reducing agent.

53. The composition of matter claim 52,

wherein said at least one photon reducing agent has an absorption spectrum that overlaps with the emission or excitation spectrum of said at least one photon producing agent.

54. The composition of matter claim 53,

wherein said at least one photon reducing agent is present in said aqueous solution at a concentration that reduces undesired fluorescence from said aqueous solution by at least 40% compared to undesired fluorescence of said aqueous solution in the absence of said at least one photon reducing agent.

55. The composition of matter of claim 54,

wherein said at least one photon reducing agent has solubility in water of about 100mM or more.

56. The composition of matter of claim 49,

wherein said at least one photon reducing agent has an absorption spectrum that overlaps with the emission or excitation spectrum of said at least one photon producing agent.

57. The composition of matter of claim 56,

wherein said at least one photon reducing agent has an extinction coefficient of at least 10,000 $M^{-1}cm^{-1}$.

58. The composition of matter claim 56,

wherein said membrane compartment is a living cell.

59. The composition of matter of claim 58,

wherein said at least one photon reducing agent is not acting as a pH indicator dye and said at least one photon reducing agent has an absorbance spectrum that over laps with the emission or excitation spectrum of said at least one photon producing agent in said aqueous solution.

60. The composition of matter of claim 49,

wherein said at least one photon producing agent in said aqueous solution can transfer energy to said at least one photon reducing agent.

61. The composition of matter of claim 49,

wherein said at least one photon reducing agent has an extinction coefficient of at least 10,000 $M^{-1}cm^{-1}$ and is present at a concentration of at least about 0.1 mM.

62. The composition of matter claim 60,

wherein said membrane compartment is a living cell and said at least one photon reducing agent is a dye.

63. The composition of matter claim 62,

wherein said living cell is a member of a plurality of living cells in a volume less than about 5 microliters.

64. The composition of matter claim 62,

wherein said composition further includes a microplate and said living cell is a member of a plurality of living cells in a well of said microplate.

65. The composition of matter claim 64,

wherein said microplate has 864 or greater wells.

66. The composition of matter claim 49,

wherein said composition further comprises a system to launch light of a predetermined wavelength through the bottom of an assay surface, wherein said predetermined wavelength is an excitation wavelength for said at least one photon producing agent.

67. The composition of matter claim 49,

wherein said at least one photon reducing agent is relatively more membrane impermeant than said at least one photon producing agent.

68. The composition of matter claim 67,

wherein said at least one photon reducing agent is present in said aqueous solution at a concentration that reduces fluorescence from said aqueous solution by at least 75% compared to fluorescence of said aqueous solution in the absence of said at least one photon reducing agent.

69. The composition of matter claim 49,

wherein said composition of matter further comprises a second photon producing agent that is a test chemical that is free in said aqueous solution.

70. A composition of matter, comprising:

a) at least one photon producing agent internalized in a living cell in optical contact with a solid surface that can pass light of a predetermined wavelength that sufficiently overlaps with the excitation spectrum of said at least one photon producing agent to excite said at least one photon producing agent, and

b) at least one photon reducing agent in an aqueous solution surrounding said living cell,

wherein said at least one photon reducing agent has an absorption spectra that overlaps with the absorption, emission or excitation spectra of said at least one photon producing agent.

71. A method of identifying a chemical with a biological activity, comprising:

a) contacting a sample with a test chemical, said sample comprising a target,

b) contacting said sample with at least one photon reducing agent, wherein said sample comprises a membrane compartment in contact with a solid surface,
wherein said membrane compartment includes at least one photon producing agent that directly or indirectly monitors the activity of said target and said at least one photon reducing agent is in an aqueous solution that contacts the outer surface of said membrane compartment, and

c) detecting an optical signal from said at least one photon producing agent,
wherein said at least one photon reducing agent has an absorption spectra that overlaps with the absorption, emission or excitation spectrum of said at least one photon producing agent
or wherein said at least one photon producing agent can exhibit fluorescence resonance energy transfer with said at least one photon reducing agent.

72. A therapeutic compound identified by a method comprising the steps of:

a) contacting a sample with a test chemical, said sample comprising a target,

b) contacting said sample with at least one photon reducing agent,

wherein said sample comprises a membrane compartment in contact with a solid surface,

wherein said membrane compartment includes at least one photon producing agent that directly or indirectly monitors the activity of said target and said at least one photon reducing agent is in an aqueous solution that contacts the outer surface of said membrane compartment, and

c) detecting an optical signal from said at least one photon producing agent,

wherein said at least one photon reducing agent has absorption spectra that overlaps with the absorption, emission or excitation spectrum of said at least one photon producing agent or wherein said at least one photon producing agent can exhibit fluorescence resonance energy transfer with said at least one photon reducing agent.

73. The therapeutic compound of claim 72,

further comprising a pharmaceutically acceptable carrier.

74. A system for identifying a chemical with a biological activity, comprising:

a) a storage and retrieval module for storing a plurality of chemicals in solution in addressable chemical wells, a chemical well retriever, and having programmable selection and retrieval of said addressable chemical wells, and having a storage capacity for at least 100,000 said addressable wells,

wherein at least one of said addressable wells comprises a photon reducing agent,

b) a sample distribution module comprising a liquid handler to aspirate or dispense solutions from selected said addressable chemical wells, said chemical distribution module having programmable selection of, and aspiration from, said selected addressable chemical wells and programmable dispensation into selected addressable sample wells, and said liquid handler can dispense into arrays of addressable wells with different densities of addressable wells per centimeter squared,

c) a sample transporter to transport said selected addressable chemical wells to said sample distribution module and optionally having programmable control of transport of said selected addressable chemical wells,

d) a reaction module comprising either a reagent dispenser to dispense reagents into said selected addressable sample wells or a fluorescent detector to detect chemical reactions ins said selected addressable sample wells, and

e) a data processing and integration module,

wherein said storage and retrieval module, said sample distribution module, and said reaction module are integrated and programmably controlled by said data processing and integration module; and said storage and retrieval module, said sample distribution module, said sample transporter, said reaction module

and said data processing and integration module are operably linked to facilitate rapid processing of said addressable sample wells.

75. The system of claim 74,

wherein said addressable chemical wells are within at least one multi-well platform.

76. The system of claim 74,

wherein said multi well platform comprises between about 96 wells and about 5000 wells.

77. The system of claim 76,

wherein the number of wells in said multi well platform is a multiple of 96.

78. A method of identifying a chemical with a toxicological activity, comprising:

contacting a sample with a test chemical, said sample comprising a target and at least one photon producing agent,

contacting said sample with at least one photon reducing agent,

detecting an optical signal from said at least one photon producing agent,

wherein said optical signal is related to a toxicological activity.

79. A method of identifying a chemical having a biological activity, comprising:

a) contacting a sample with a test chemical, said sample comprising a target,

b) contacting said sample with at least one photon reducing agent, wherein said sample comprises a membrane compartment, wherein said membrane compartment includes at least one photon producing agent that directly or indirectly monitors the activity of said target and said at least one photon reducing agent is in an aqueous solution that contacts the outer surface of said membrane compartment, and

c) detecting an optical signal from said at least one photon producing agent by FACS.